


Systematic Review

Clinical Applications of Three-Dimensional Printing in Otolaryngology–Head and Neck Surgery: A Systematic Review

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Objectives: Medical three-dimensional (3D) printing, the fabrication of handheld models from medical images, has the potential to become an integral part of otolaryngology–head and neck surgery (Oto-HNS) with broad impact across its subspecialties. We review the basic principles of this technology and provide a comprehensive summary of reported clinical applications in the field.

Methods: Standard bibliographic databases (MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, Web of Science, and The Cochrane Central Registry for Randomized Trials) were searched from their inception to May 2018 for the terms: “3D printing,” “three-dimensional printing,” “rapid prototyping,” “additive manufacturing,” “computer-aided design,” “bioprinting,” and “biofabrication” in various combinations with the terms: “ptolaryngology,” “head and neck surgery,” and “otology.” Additional articles were identified from the references of retrieved articles. Only studies describing clinical applications of 3D printing were included.

Results: Of 5,532 records identified through database searching, 87 articles were included for qualitative synthesis. Widespread implementation of 3D printing in Oto-HNS is still at its infancy. Nonetheless, it is increasingly being utilized across all subspecialties from preoperative planning to design and fabrication of patient-specific implants and surgical guides. An emerging application considered highly valuable is its use as a teaching tool for medical education and surgical training.

Conclusions: As technology and training standards evolve and as healthcare moves toward personalized medicine, 3D printing is emerging as a key technology in patient care in Oto-HNS. Treating physicians and surgeons who wish to stay abreast of these developments will benefit from a fundamental understanding of the principles and applications of this technology.

Key Words: Three-dimensional printing, additive manufacturing, rapid prototyping, otolaryngology–head and neck surgery applications, ear-nose-throat applications.

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Additional supporting information may be found online in the Supporting Information section at the end of the article.

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INTRODUCTION

Medical three-dimensional (3D) printing—the fabrication of hand-held models from medical images—has become an integral part of medical practice, being rapidly incorporated into academic curricula, residency training, and delivery of healthcare.^{1,2} 3D-printed models can mimic all shapes and forms necessary in real patient anatomies, serving to improve patient care, surgical outcomes, and resident education. In otolaryngology–head and neck surgery (Oto-HNS), 3D printing is being increasingly utilized to fabricate life-size training models, tissue scaffolds, as well as patient-specific implants and surgical guides.³ This can theoretically provide a much more effective method of delivering healthcare, and the technology has the potential to hold a key role in the field of Oto-HNS with broad impact across its sub-specialties.³

In this article, we aimed to review clinical applications of 3D printing as the usage and complexity of 3D printing in Oto-HNS continues to grow. Several studies have described otolaryngologic applications of 3D printing; however, no comprehensive systematic review of the standard bibliographic literature has yet taken place. The

purpose of this systematic review was two-fold: 1) to provide a comprehensive summary of reported clinical applications of 3D printing across all subspecialties within Oto-HNS and 2) to identify evidence gaps that will guide future research in 3D printing in Oto-HNS. Basic principles of the technology as well as current limitations and future directions are also described.

MATERIALS AND METHODS

We performed a systematic review based on an a priori protocol that was registered with PROSPERO (CRD42016051370), the international prospective register of systematic reviews.⁴ This study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.⁵

Search Design

Standard bibliographic databases (MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, Web of Science, and The Cochrane Central Registry for Randomized Trials) were searched from their inception to May 2018. The following Medical Subject Headings and keywords were used: “3D printing,” “three-dimensional printing,” “rapid prototyping,” “additive manufacturing,” “computer-aided design,” “bioprinting,” and “biofabrication” in various combinations with “otolaryngology,” “head and neck surgery,” and “otology.” The reference lists of articles returned by the search and relevant review articles were screened to identify any additional studies that were not identified by the search.

Selection Criteria

Two independent reviewers (C.J.H. and B.Y.H.) screened the titles and abstracts of the retrieved articles for their potential relevance. The full-text versions of all potentially relevant articles were then assessed using a preestablished eligibility form based on our inclusion and exclusion criteria described below. Any discrepancies were settled by consensus and discussion amongst the reviewers. Studies considered for inclusion were clinical studies written in English that described otolaryngologic applications of 3D printing in humans. Review articles, abstracts, letters, commentaries, and simulation studies were excluded. Studies that did not have direct clinical applications (e.g., technique/model development) were also excluded.

Data Extraction, Quality Assessment, and Statistical Analyses

The same two reviewers (C.J.H. and B.Y.H.) extracted data independently by using a preestablished data extraction form. Data extracted were as follows: title, first author, year of publication, general study and patient characteristics, study methods, and outcome definitions and data. Discrepancies were settled by consensus and discussion amongst the reviewers. The same reviewers were also involved in assessing the quality of the included studies. Strength and risk of bias assessments were done using recently improved methodological principles including the Newcastle-Ottawa Scale⁶ and the Cochrane risk of bias tool.⁷ The frequency of 3D printing publications over time was also assessed by linear regression. In addition, the proportion of 3D printing publications for each article type and for each subspecialty was calculated.

RESULTS

Our search identified 5,532 records, 261 of which remained after removing duplicate entries and excluding noneligible articles from title and abstract screening (Fig. 1). After application of our inclusion criteria by reviewing these potential articles in full-text, 87 articles were included for qualitative synthesis (see Supporting Information, Appendix 1, in the online version of this article). Meta-analysis was not possible due to heterogeneity in outcome reporting.

Table I represents study characteristics of the included studies. There were a total of 710 patients included in our study. For the 480 patients for which gender was specified, 295 were males and 185 were females. The mean age of included patients was 42.8 years (range, 0.25–84 years). The five most common disease entities (n = number of patients) in which 3D printing was utilized were microtia (n = 94) and squamous cell carcinoma (n = 87), followed by orbital wall/floor trauma (n = 76), ameloblastoma (n = 42), and osteoradionecrosis (n = 35). The most common procedures (n = number of patients) in which 3D printing was utilized were mandibular resection and reconstruction (n = 251), followed by auricular reconstruction (n = 92), orbital reconstruction (n = 84), maxillary resection and reconstruction (n = 49), and mandibular open reduction and internal fixation (n = 25).

The majority of included studies were from head and neck (H&N) (36%) and facial plastics (36%), followed by pediatric otolaryngology (9%) (Table I). The majority of included studies were case reports (53%) followed by case series (26%) and cross-sectional studies (7%) (Table I). Of note, randomized controlled trials made up only 6% of the total number of included studies. The number of articles relating to 3D printing tended to increase over time (Fig. 2).

Examples of 3D Printing Clinical Applications in Oto-HNS

H&N. Surgical management of H&N diseases requires precise understanding, access, and replication of complex anatomy. 3D-printed implants have gained popularity amongst H&N surgeons in recent years, as 3D-printed models can provide the surgeon with a customized fit,^{3,8} accounting for variations in patient anatomy.

The most widely used application of 3D printing in H&N today is in preoperative planning. 3D models can exemplify anatomical structures of interest and benefit surgeons by providing preoperative simulation that allows for more precise surgical approaches.⁹ They have been shown to enhance tactile sensory input, provide a better understanding of delicate nearby structures such as nerves and vessels, and minimize unnecessary procedures, all of which may translate to reduced perioperative complications. 3D printing of customized surgical templates and equipment further optimize operative interventions. For instance, the use of prebent reconstruction plates has been extensively documented in the literature.^{10–14} Using 3D rapid prototyping technology, Ro and colleagues¹³ and Prisman and colleagues¹⁴ investigated the value of preoperative mandibular contouring in patients undergoing reconstruction of the

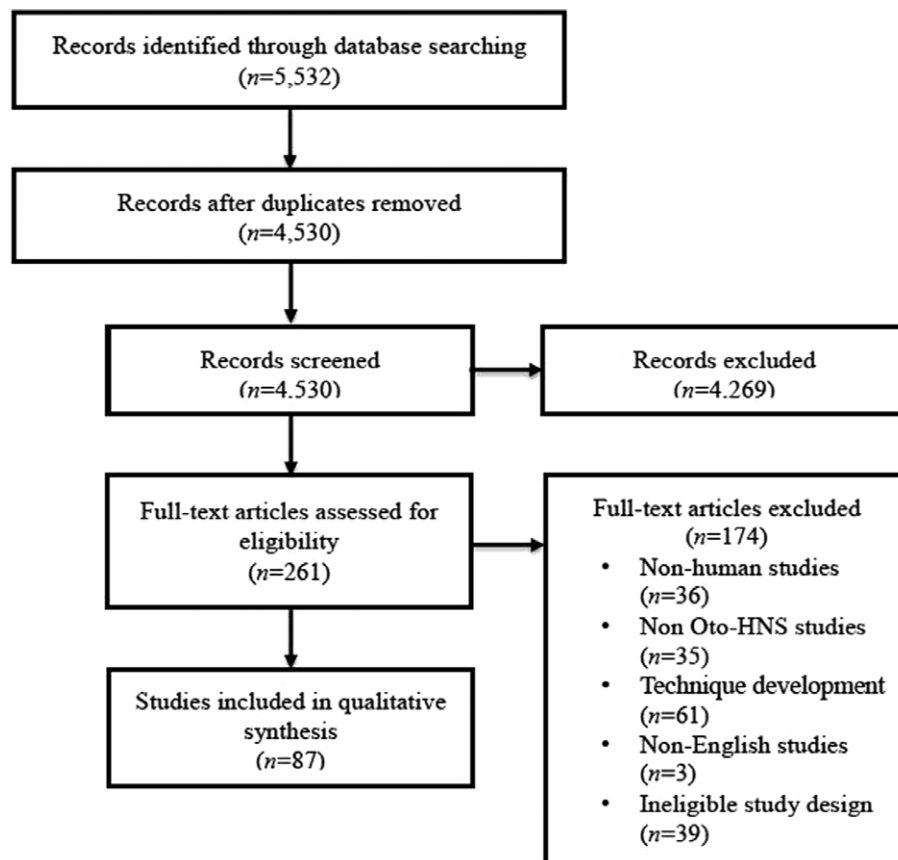


Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses study flow diagram. Oto-HNS = otolaryngology–head and neck surgery.

mandible with osseous free flap reconstruction. They both reported that preoperative contouring was beneficial in restoring the contour of the mandible postoperatively. Moreover, Ro and colleagues¹³ found that this approach decreased operative time and provided a reconstructive method for tumors that extended lateral to the buccal soft tissues. In oromandibular reconstruction, a 3D-printed versatile surgical platform (V-stand) has also been utilized, serving as a template to provide an excellent means for accurate spatial positioning of a fibular free flap during surgery.¹⁵

Another common use of 3D printing in H&N cancer surgery is in reconstruction of bony defects, especially following mandibular resection. Using rapid prototyping, custom mandible titanium trays have been designed, printed, and implanted, followed by autogenous bone grafting.^{16–18} Satisfactory aesthetic results including symmetry and quality of contour were achieved in all three studies with no reported severe complications. The potential benefits of 3D printing in H&N cancer include improved surgical planning, decreased operative time, and more accurate reconstruction.¹⁹

Otology. Otolologists often face challenges related to intricate pathologic states. In this context, the true 3D visualization provided by 3D-printed models offers great potential as a tool for improved treatment planning. Although much of the otologic applications to date have been in surgical

education of trainees, namely in temporal bone dissection, 3D printing is increasingly being utilized to develop patient-specific 3D-printed models for preoperative otologic surgical planning and simulation. Suzuki and colleagues,²⁰ for instance, created a laser-sintered 3D model to aid surgery for recurrent cholesteatoma involving complex bony structures and soft tissue, and found that the model allowed for optimal surgical planning. Rose and colleagues²¹ similarly produced a physical model based on their patient's preoperative CT scan, and the model was used to simulate tympanomastoidectomy for a complicated recurrent cholesteatoma. Temporal bone models have also been 3D printed and used as beneficial adjuncts for preoperative planning and simulation for the repair of tegmen tympani defects.²²

Rhinology and skull base. Rhinology and skull base surgery poses unique operative challenges due to complex and variable anatomy, and the risk of major complications. It requires careful appreciation of the pathology preoperatively, a clear understanding of the techniques available for correction, a proposed plan of action and sequence, and a meticulous, uncompromising execution of the surgical technique. In the management of petroclival tumors, Muelleman and colleagues²³ produced patient-specific 3D models for preoperative petroclival tumor resection planning, and these models were used to measure the fidelity of printed anatomical structures and compare tumor

Total no. of included patients	710
Gender	295 males and 185 females (out of 480 patients)
Mean age, yr (range)	42.8 (0.25–84)
Five most common disease entities in which 3D printing was utilized (no. of patients)	Microtia (94) Squamous cell carcinoma (87) Orbital wall/floor trauma (76) Ameloblastoma (42) Osteoradionecrosis (35)
Five most common procedures in which 3D printing was utilized (no. of patients)	Mandibular resection and reconstruction (251) Auricular reconstruction (92) Orbital reconstruction (84) Maxillary resection and reconstruction (49) Mandibular ORIF (25)
Subspecialty breakdown of included studies (%)	Head and neck (36%) Facial plastics (36%) Pediatrics (9%) Medical education (7%) Rhinology and skull base (6%) Otology (4%) Laryngology (2%)
Study design (%)	Case report (53%) Case series (26%) Cross-sectional (7%) RCT (6%) Prospective cohort (4%) Retrospective cohort (1%) Case control (1%) Historical cohort (1%) Single-arm trial (1%)

3D = three-dimensional; ORIF = open reduction and internal fixation; RCT = randomized controlled trial.

exposures afforded by different approaches. The authors found the 3D-printed models quite useful for preoperative planning as they provided authentic replicas of petroclival tumors in relation to bony structures. In osteoplastic flap frontal sinus surgery, Daniel and colleagues²⁴ produced onlay frontal sinus templates from computed tomography data of patients and used them intraoperatively on a series of 10 patients with greater than 1 mm accuracy. 3D-printed templates have also been used in septal prosthesis sizing and resulted in 90% retention rate of prosthesis used to close nasal septal perforations.²⁵

Pediatric otolaryngology. Advanced imaging, preoperative planning, and fabrication of implants with 3D printing have a growing potential in pediatric otolaryngology as the field involves all aspects of Oto-HNS including complex airway cases, surgical rehabilitation of hearing loss, and endoscopic sinus surgery. 3D printing in pediatric otolaryngology was initially employed by Zopf and colleagues,²⁶ who created a 3D model of the tracheobronchial tree of a patient with severe bronchomalacia, allowing the authors an opportunity to practice orientation and placement of a 3D-printed airway splint. Since then, 3D printing is rapidly gaining interest amongst Oto-HNS surgeons and radiologists providing care to children, especially in the management of complex airway cases. 3D printing technology has since been successfully applied in the production of personalized medical devices for the treatment of tracheobronchomalacia. Morrison and colleagues²⁷ created and implanted patient-specific 3D-printed external airway splints in three infants with severe tracheobronchomalacia, and these splints were able to accommodate airway growth while preventing external compression before being bioresorbed over time. All patients demonstrated resolution of both pulmonary and extrapulmonary complications of tracheobronchomalacia following external airway splinting.

In addition, the technology has been recently utilized to facilitate the multidisciplinary approach to perinatal management of complex airway anomalies in a newborn.²⁸

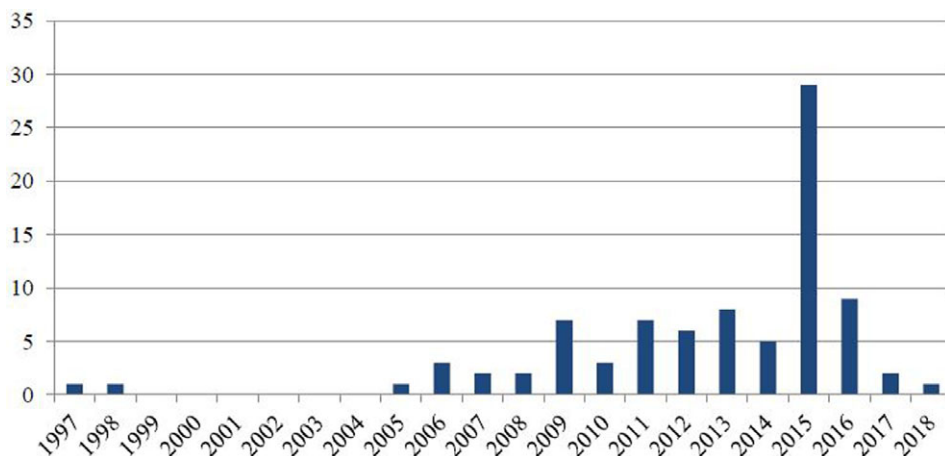


Fig. 2. Number of three-dimensional printing publications in otolaryngology-head and neck surgery. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Complex fetal maxillofacial anatomy was 3D printed based on fetal magnetic resonance imaging, and the 3D model was able to reveal the relationship of the facial soft tissue mass to the maxillomandibular skeleton and guide the appropriate airway management plan before delivery.²⁸ Beside complex airway cases, 3D printing has also been utilized to print a pediatric temporal bone model of petrous apex cholesterol granuloma to successfully plan total endoscopic permeal drainage of the cystic lesion.²⁹

Facial plastics. In facial plastics, 3D laser surface scanning and rapid prototyping have been utilized to develop translucent templates for intraoperative use to accurately recreate the dimensions of the nasal tip and dorsum with rib and ear cartilage.³⁰ Similarly, a rapid prototyping system has been used to 3D print a three-part surgical template for use in positioning of craniofacial implants for supporting a total nasal prosthesis in a patient who suffered a total loss of his nose due to a gunshot wound.³¹ Auricular prostheses have also been 3D printed and used on patients with missing ears. A female patient with grade 4 microtia and a male patient who underwent surgical resection for basal cell carcinoma, respectively, had auricular prostheses 3D printed and permanently placed.^{32,33} The use of 3D-printed ear models as templates for auricular reconstruction in patients with microtia has been extensively documented in the literature.^{34–37} In addition, 3D-printed models are routinely used to prebend titanium mesh for orbital reconstruction following orbital wall/floor trauma.^{38–40}

Medical Education, Surgical Training, and Informed Consent

3D-printed models have emerged as important teaching aids in all levels of medical and residency training, and are likely to have further potential applications and benefits in the future. Although using cadaveric models has several important advantages including anatomical fidelity and a relatively low cost, they are limited by several factors, including the inability to demonstrate specific pathologic states. Certain pathologies are rare or cannot be sufficiently preserved at the time of prosection.^{41,42} Despite the low cost of storing human cadavers, medical schools and residency programs find prosecting, handling, and disposing the specimens difficult and expensive.⁴³ 3D printing has emerged as a new supplemental tool in the training of students and residents. This alternative approach to fabricate anatomically accurate models is advantageous over cadavers and current simulation models because it allows for the rapid production of multiple complex body parts.⁴³

3D printing is already gaining ground in the surgical training field, and Oto-HNS is no exception. 3D-printed models have been used to perform common navigation maneuvers and presurgical planning in various subspecialties, opening new avenues for their use as surgical training tools. 3D-printed models have already been shown to be effective for training in temporal bone simulation^{44,45} as well as in training of microtia⁴⁶ and endoscopic endonasal surgery.^{10,47}

Recently, Al-Ramahi and colleagues⁴⁸ developed a 3D-printed airway model for rigid bronchoscopy foreign body removal training. When compared with a traditional porcine model, this 3D model has proven to be an excellent alternative with satisfactory simulation of the size and mechanical properties of various age groups. 3D printing was also recently utilized by Chiesa Estomba and colleagues⁴⁹ to create an epistaxis training model, where the residents were able to practice identifying and treating sources of bleeding with nasal packing materials.

3D-printed models can facilitate the process of obtaining an informed consent prior to a surgical intervention. They provide patients and their families with a better understanding of the disease and planned procedures using realistic representations.^{50,51} In addition, patients have reported a high degree of satisfaction from increased patient education and involvement.⁵² 3D-printed models can also optimize preoperative planning by allowing surgeons to devise patient-specific treatment strategies.

DISCUSSION

Our study aimed to provide a synthesis of the available clinical applications of 3D printing across all Oto-HNS subspecialties. As demonstrated in our review, widespread implementation of 3D printing in Oto-HNS is still at its infancy, with a lack of comparative studies, small sample sizes, and heterogeneous outcome reporting (see Supporting Information, Appendices 2–4, in the online version of this article). However, it is emerging as a key technology in patient care in Oto-HNS and is also proving to be highly valuable in its use as a teaching tool and surgical training.

In more recent years, complex printing of viable tissues and organs has been explored as another potential application of 3D printing. Also known as bioprinting, it refers to the utilization of 3D printing technologies to combine cells, growth factors, and biomaterials to fabricate desired cell patterns that best resemble natural tissues and/or organs with humanlike morphology and histology.^{53,54} 3D bioprinting utilizes the layer-by-layer method to deposit cells or extracellular matrix to create a desired tissue or organ construct that can later be incorporated into patients.⁵⁴ Bioprinting is highly promising in the field of 3D printing, as soft tissue printing can, for instance, improve different types of reconstructive surgeries following head and neck cancer ablation by maintaining adjacent soft tissue structures. Early in vitro and in vivo reports have demonstrated satisfactory results in bioprinting thus far. In one animal study, 3D-printed scaffolds coated with mesenchymal stem cells seeded in fibrin were experimented with for the repair of partial tracheal defects in four rabbits. The shape and function of reconstructed trachea using 3D-printed artificial tracheal grafts were restored successfully without any graft rejection.⁵⁵ Goldstein and colleagues⁵⁶ similarly ran an in vitro and in vivo pilot animal study for the creation of a graft for laryngotracheal reconstruction. The authors demonstrated that 3D-printed, tissue-engineered grafts for laryngotracheal reconstruction retained their cartilaginous properties in vitro and in vivo and may have future applications in airway reconstruction. A tissue-engineered trachea developed recently has a

mechanical behavior similar to native trachea and may have a future role in reconstruction of tracheal stenosis.⁵⁷ Human turbinate mesenchymal stromal cell sheets on the luminal surface of a tissue-engineered tracheal graft can accelerate the tracheal epithelial regeneration, and the tissue-engineered tracheal graft with human turbinate mesenchymal stromal cell sheets may be beneficial in tracheal epithelial regeneration.⁵⁸ Bioprinting also has been applied in an experimental animal model of augmentation rhinoplasty. In 2015, Kim and colleagues⁵⁹ evaluated the feasibility of using 3D-printed polycaprolactone scaffold seeded with fibrin/chondrocytes as a potential dorsal augmentation material for rhinoplasty. Throughout the experimental period, rabbits in which the constructs were implanted maintained the initial augmentation level with no postoperative complications. Although many of the bioprinting technologies are still in their infancy, they could have significant future impact in managing several Oto-HNS challenges, including the treatment of congenital anomalies, reconstruction of cancerous defects, and the correction of airway defects.

3D-printed handheld devices, customized prostheses, and 3D surgical templates and implants can be derived from any imaging modality, including, but not limited to, computed tomography and magnetic resonance imaging. Generating an accurate 3D-printed model requires the generation of unique printable file formats recognized by 3D printers. For instance, starting with standard Digital Imaging and Communication in Medicine (DICOM) image files from computed tomography or magnetic resonance imaging scans, initial postprocessing involves the segmentation (i.e., demarcation of individual voxels in the images) of the DICOM images into individual 3D-printable parts (i.e., individual tissues) and subsequently their conversion into a file format readable by 3D printers such as the Standard Tessellation Language (STL) file format. Tissue models stored in STL files can then be further processed to undergo additional refinements such as closing gaps due to imperfect segmentation (e.g., wrapping), smoothing to reduce the effects of image noise, and trimming to highlight the desired anatomy. These post-processing steps are performed using computer-aided design (CAD) software. This additional refinement process is often crucial to ensure successful printing of 3D models, and to ensure that these models—once printed—have maximum utility in a clinical setting. The wrapping and smoothing functions on CAD software specifically allow elimination of surface imperfections in 3D models by creating watertight surfaces and decreasing the amount of noise introduced during the scanning process. A number of other postprocessing steps also exist in CAD software, including the ability to design implantable devices that precisely fit the segmented tissues and the extrusion of luminal tissues to create shells (e.g., for 3D printing of hollow blood vessels from angiographic images). Once 3D STL models have been edited using CAD software, they can ultimately be fabricated by depositing material layer-by-layer to build a 3D object using diverse 3D printing techniques, such as stereolithography, material jetting, selective laser sintering, binder jetting, and fused deposition modeling. Further details regarding the workflow of 3D printing can be found elsewhere.²

Limited awareness and lack of surgeon/radiologist experience account for the current lack of widespread adaptation of this technology in the management of Oto-HNS pathologies. Although 3D printing is expected to eventually play a key role in patient care, many applications of 3D printing in Oto-HNS are still in their infancy, with only early, scarce data available. It should be noted that a large portion of the articles published to date are case reports and have not been validated by large-scale studies or randomized controlled trials. Although the potential implications of these individual case reports are encouraging, large-scale clinical studies are required to determine the true clinical efficacy of this technology. Until then, caution should continue to be exercised when incorporating 3D printing into clinical practice.

There is currently a substantial financial cost associated with investing in 3D printing technologies, and the current lack of reimbursement poses a challenge for early adopters among otolaryngologists. These costs, however, can be expected to drop substantially with time, and reimbursements for 3D-printed models for medical use may follow in the near future. Although the cost-effectiveness of 3D printing can only be ascertained after widespread adoption and use, there is recent evidence that using 3D-printed models can be a cost-saving measure.¹⁹ It has also been reported that the creation of 3D models may reduce operating time, which may reduce blood loss, wound exposure, and duration of anesthesia.¹⁶ It is likely that the initial investment in 3D printing makes it difficult to adopt the technology at present for otolaryngologists practicing on an individual basis; however, the use of these models will increase when amortized over the life of the device and as they gain acceptance as evidence-based data expand. The customizability of 3D printing also continues to pose unique challenges for regulatory bodies to ensure quality control of these devices. To provide some regulation over 3D-printed materials, the Food and Drug Administration recently published a document to assist in the adoption of 3D printing technologies.⁶⁰ However, as the use of 3D printing begins to expand in the field of Oto-HNS, the accompanying regulations will continue to evolve.⁶¹ The readers of this article are advised to consult their local regulatory bodies when incorporating patient-specific 3D-printed models into their clinical practice.⁶⁰

An important limitation of this review is that we only included studies that describe clinical applications of 3D printing, and therefore it does not represent the total number of 3D printing publications in Oto-HNS. Additionally, in a number of studies, it was difficult to categorize studies into a particular subspecialty, as more than one subspecialty may perform a given procedure, and the subspecialty groupings may change depending on one's institution.

CONCLUSION

3D printing is increasingly being utilized in Oto-HNS across all subspecialties from preoperative planning to design and fabrication of patient-specific implants and surgical guides. As technology and training standards evolve and as healthcare moves toward personalized medicine,

3D printing will likely emerge as a key technology in patient care in Oto-HNS. Otolaryngologists who wish to stay abreast of these developments would benefit from a fundamental understanding of the principles and applications of this technology.

Acknowledgments

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